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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/539,725	06/20/2005	Ralf Reski	GRNO-01U1	7533
59538 7590 08/13/2009 BIOTECH BEACH LAW GROUP, PC 625 BROADWAY Suite 1210 SAN DIEGO, CA 92101				
EXAMINER RAGHU, GANAPATHIRAM				
ART UNIT		PAPER NUMBER		
1652				
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08/13/2009		PAPER		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/539,725

Applicant(s)

RESKI ET AL.

Examiner

GANAPATHIRAMA RAGHU

Art Unit

1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 July 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 38-40, 42, 48, 50, 78, 81-87 and 96 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 38-40, 42, 78, 81-87 and 96 is/are rejected.
- 7) ☒ Claim(s) 48 and 50 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date 07/13/09.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

Application Status

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 07/13/09 has been entered.

In response to the Final Office Action dated 01/13/09, applicants filed an RCE received on 07/13/09 is acknowledged. Applicants have amended claims 38 and 81, cancelled claims 88-95 added new claim 96. Claims 38-40, 42, 48, 50, 78, 81-86 and 96 are pending and are under consideration in the instant Office Action.

Objections and rejections not reiterated from previous action are hereby withdrawn.

Withdrawn- Claim Rejections: 35 USC § 112-First Paragraph

Previous rejection of claims 38-40, 42, 48, 50, 78 and 81-87 rejected under 35 U.S.C. 112, first paragraph, for enablement and written description is being withdrawn due to amendments to claims and persuasive arguments.

Specification-Objections

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is suggested "Transformed bryophyte cell expressing enzymes involved in glycosylation for the production of heterologous glycosylated proteins".

New-Claim Objections

Claims 40, 42, 78, 83, 84 and 87 are objected to because of the following informality:

Applicants are advised that should claims 40, 42 and 78 are found allowable, claims 83, 84 and 87 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof, as claim 84 is identical in scope to claim 40; as claim 83 is identical in scope to claim 42; and as claim 87 is identical in scope to claim 78. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

New-Double Patenting rejection

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 38-40, 42, 78, 81, 83, 84 and 89 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7, 16, 23, 24, 28 and 29 over co-pending US application 11/995,191. An obviousness-type double patenting rejection is appropriate where the conflicting claims

are not identical, but an examined application claim is not patentably distinct from the reference claim, because the examined claim is either anticipated by, or would have been obvious over reference claim. See, e.g., *In re Berg*, 140 F.3d 1428,46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir.1993); *In re Longi* 759 F.2d 887,225 USPQ 645 (Fed. Cir. 1985).

Although, the conflicting claims are not identical, they are not patentably distinct from each other. Claims 38-40, 42, 78, 81, 83, 84 and 89 of the instant application and claims 1-7, 16, 23, 24, 28 and 29 of the reference US application 11/995,191 are both directed to same population of transformed bryophyte cells, said bryophyte cells comprising a disrupted endogenous fucosyltransferase and/or xylosyltransferase and comprising nucleotide sequences encoding enzymes involved in mammalian/human glycosylation pattern. Specifically *Physcomitrella patens* bryophyte cells of claims 38-40, 42, 78, 81, 83, 84 and 89 of instant application expressing a functional human beta 1,4 galactosyltransferase involved in human glycosylation pattern is the same population of transformed bryophyte cells of claims 1-7, 16, 23, 24, 28 and 29 over co-pending US application 11/995,191. Claims 38-40, 42, 78, 81, 83, 84 and 89 of the instant application listed above cannot be considered patentably distinct over claims 1-7, 16, 23, 24, 28 and 29 over co-pending US application 11/995,191 when there is specifically recited embodiment that would mainly anticipate claims 38-40, 42, 78, 81, 83, 84 and 89 of the instant application. Alternatively, claims 38-40, 42, 78, 81, 83, 84 and 89 of the instant application cannot be considered patentably distinct over claims 1-7, 16, 23, 24, 28 and 29 of the reference US application 11/995,191, when there is

specifically disclosed embodiment that supports claims 1-7, 16, 23, 24, 28 and 29 of that reference US application 11/995,191 and falls within the scope of the claims 38-40, 42, 78, 81, 83, 84 and 89 herein, because it would have been obvious to one having ordinary skill in the art to modify claims 1-7, 16, 23, 24, 28 and 29 of that reference US application 11/995,191 by selecting a specifically disclosed embodiment that supports those claims i. e., A transformed bryophyte cell that comprises six heterologous nucleotide sequences each operably linked to an exogenous promoter that drives expression in the bryophyte cell... One of ordinary skill in the art would have been motivated to do this because that embodiment is disclosed as being preferred embodiment within claims 1-7, 16, 23, 24, 28 and 29 of co-pending US application 11/995,191.

New-Claim Rejections 35 USC § 112-Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Upon further review, claims 40 and 84 and claims 85-86 depending from claim 84 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 40 and 84 recites the phrase "human glycosylation patterns". It is unclear to the examiner as to what biological or chemical or physical characteristics define a "human glycosylation pattern". Examiner seeks clarification as prior art teaches the oligosaccharides found on glycoproteins vary for example: N-glycosylation, O-glycosylation and carbohydrates that are also components of glycoposphatidylinositol

anchor used to secure proteins to cell membranes (see Jenkins et al., Nature Biotechnol., 1996, Vol. 14: 975-981 Fig. 1, page 976), and as such show varying patterns of glycosylation. In the light of the above teachings, it is unclear to the examiner as to what biological or chemical or physical-structural features/patterns characteristics define a "human glycosylation pattern". Clarification and correction required.

Claims 78 and 87 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949).

In the present instance, claims 78 and 87 recites the broad recitation "A bryophyte plant or bryophyte tissue, and the claim also recites "a transformed bryophyte cell according to claim 38 which is *Physcomitrella patens*" which is the narrower statement of the range/limitation, furthermore, it is not clear to the examiner whether applicants are claiming a chimeric bryophyte plant or tissue other than "transformed *Physcomitrella patens* of claim 38". Clarification and correction required.

Claim 96 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 96 recites "GenBank under accession number AJ429145 and GenBank under accession number AJ429144" in the claim. As GenBank sequences are constantly curated and updated, it is not clear to the examiner which version of the said sequence the applicants' intend to encompass in the claim. Examiner suggests that the applicants' may overcome this rejection by amending the specification to include the actual sequences of the "GenBank under accession number AJ429145 and GenBank under accession number AJ429144" recited in the specification along with providing an affidavit attesting that the submitted sequences are the sequence version of that database that was contemporaneous with the submission of the application and assign a SEQ ID NO: or if a SEQ ID NO: is already assigned to said sequences applicant's are urged to replace the "GenBank under accession number AJ429145 and GenBank under accession number AJ429144" with respective SEQ ID NO. Clarification and correction is required.

New-Claim Rejections: 35 USC § 112-First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

Claims 40, 42, 78 and 83-87 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a specific bryophyte *Physcomitrella patens* wherein in said *Physcomitrella patens* the endogenous gene encoding for alpha 1, 3-fucosyltransferase (FucT, 1711 bp, GenBank: partial cDNA: AJ429145, page 32 of specification) disrupted through targeted insertion by primer sequences SEQ ID NO: 48, 49, 50 and 51 or an endogenous gene encoding for beta 1,2 xylosyltransferase (XylT, 1788 bp, GenBank: corresponding to the coding region: AJ429144, page 38 of specification) disrupted through targeted insertion by primer sequences SEQ ID NO: 67, 68, 69 and 70 (page 39 of specification) or a double knockout comprising said FucT and XylT disrupted through targeted insertion (double knockout, disrupting the coding regions of said genes, pages 44-45 of specification), further in said single knockout or double knockout *Physcomitrella patens* the gene encoding the human beta-1,4-galactosyltransferase catalyzing the following glycosylation pattern; UDP-galactose + N-acetyl-D-glucosaminylglycopeptide \rightleftharpoons UDP + beta-D-galactosyl 1, 4,-N-acetyl-beta-D-glucosaminylglycopeptide (GalT, GenBank X55415; page 41 of specification) has been integrated by homologous recombination and said *Physcomitrella patens* comprising said gene knockout (FucT and XylT or double knockout) expressing the human GalT is transformed with an expression construct encoding the secretable/soluble form of human vascular endothelial growth factor (VEGF) and said VEGF comprising the

specific human N-glycan glycosylation pattern as catalyzed by said GalT enzyme, **does not** reasonably provide enablement for a transformed bryophyte from *Physcomitrella patens*, i) said bryophyte cell further comprising any functional human beta-1,4-galactosyltransferase including variants, mutants and recombinants capable of producing any human glycosylation pattern (as in claims 40, 42, 83 and 84) and ii) any bryophyte plant or bryophyte tissue comprising said transformed *Physcomitrella patens* (as in claims 78 and 87; also see 112 second paragraph rejection for claim interpretation). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with the claims.

Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 40, 42, 78 and 83-87, broadly encompass: a transformed bryophyte from *Physcomitrella patens*, i) said bryophyte cell further comprising any functional human beta-1,4-galactosyltransferase including variants, mutants and recombinants capable of producing any human glycosylation pattern (as in claims 40, 42, 83 and 84) and ii) any bryophyte plant or bryophyte tissue comprising said transformed *Physcomitrella patens*

(as in claims 78 and 87; also see 112 second paragraph rejection for claim interpretation). The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to a transformed bryophyte from *Physcomitrella patens* comprising extremely large number polynucleotides and encoding polypeptides of undefined structure said polypeptides having a functional human beta-1,4-galactosyltransferase including variants, mutants and recombinants capable of producing any human glycosylation pattern and furthermore any bryophyte plant or bryophyte tissue comprising said transformed *Physcomitrella patens* as broadly encompassed by the claims.

In this case the disclosure is limited to a specific bryophyte *Physcomitrella patens* wherein in said *Physcomitrella patens* the endogenous gene encoding for alpha 1, 3-fucosyltransferase (FucT, 1711 bp, GenBank: partial cDNA: AJ429145, page 32 of specification) disrupted through targeted insertion by primer sequences SEQ ID NO: 48, 49, 50 and 51 or an endogenous gene encoding for beta 1,2 xylosyltransferase (XylT, 1788 bp, GenBank: corresponding to the coding region: AJ429144, page 38 of specification) disrupted through targeted insertion by primer sequences SEQ ID NO: 67, 68, 69 and 70 (page 39 of specification) or a double knockout comprising said FucT and XylT disrupted through targeted insertion (double knockout, disrupting the coding regions of said genes, pages 44-45 of specification), further in said single knockout or double knockout *Physcomitrella patens* the gene encoding the human beta-1,4-galactosyltransferase catalyzing the following glycosylation pattern; UDP-galactose + N-acetyl-D-glucosaminylglycopeptide \rightleftharpoons UDP + beta-D-galactosyl 1, 4,-N-acetyl-beta-D-

glucosaminylglycopeptide (GalT, GenBank X55415; page 41 of specification) has been integrated by homologous recombination and said *Physcomitrella patens* comprising said gene knockout (FucT and XylT or double knockout) expressing the human GalT is transformed with an expression construct encoding the secretable/soluble form of human vascular endothelial growth factor (VEGF) and said VEGF comprising the specific human N-glycan glycosylation pattern as catalyzed by said GalT enzyme.

The guidance provided is insufficient, as the breadth and scope of the bryophyte with regard to a transformed bryophyte from *Physcomitrella patens* comprising extremely large number polynucleotides and encoding polypeptides of undefined structure said polypeptides having a functional human beta-1,4-galactosyltransferase including variants, mutants and recombinants capable of producing any human glycosylation pattern and furthermore any bryophyte plant or bryophyte tissue comprising said transformed *Physcomitrella patens* (also see 112, second paragraph for claim interpretation). Even the applicants in the specification on page 6, lines 10-15 have admitted that N-glycosylation is very complex and well regulated as N-glycosylation depends not only on developmental stages for plants but also dependent upon culture conditions. Furthermore, the art teaches: i) the oligosaccharides found on glycoproteins vary for example: N-glycosylation, O-glycosylation and carbohydrates that are also components of glycoposphatidylinositol anchor used to secure proteins to cell membranes (see Jenkins et al., Nature Biotechnol., 1996, Vol. 14: 975-981; see Fig. 1, page 976) and as such show varying patterns of glycosylation; and ii) there is a family of GalT transferases with differing structures, substrate specificities, differing catalytic and

distinct biological functions (see Bennett et al., 1999, J. Biol. Chem., Vol. 274 (36): 25362-25370; see page 25362 columns 1 and 2) and N-glycosylation appears to involve a series of reactions catalyzed by specific glycosidases and glycosyltransferases.

Therefore a skilled artisan requires the information regarding specific genes encoding the specific polypeptides involved in the specific N-glycan synthesis. In view of the breadth of the claims, the amount of experimentation required, the lack of guidance, working examples, and unpredictability of the art in predicting with regard to a transformed bryophyte from *Physcomitrella patens* comprising extremely large number polynucleotides and encoding polypeptides of undefined structure said polypeptides having a functional human beta-1,4-galactosyltransferase including variants, mutants and recombinants capable of producing any human glycosylation pattern and furthermore any bryophyte plant or bryophyte tissue comprising said transformed *Physcomitrella patens* and as such practicing the claimed invention would require undue experimentation. As such, the specification fails to enable the entire scope of the claimed invention.

The specification does not support the broad scope of the claims because the specification does not establish: **(A)** diverse structures for human beta-1,4-galactosyltransferase including variants, mutants and recombinants capable of producing any human glycosylation pattern; **(B)** regions of the protein/polynucleotide structure which may be modified without affecting the human beta-1,4-galactosyltransferase activity; **(C)** the general tolerance of the polypeptide to modification and extent of such tolerance; **(D)** a rational and predictable scheme for

modifying any amino acid residue or the respective codon in the polynucleotide with an expectation of obtaining the desired biological function; and (E) sufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claim must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of a transformed bryophyte from *Physcomitrella patens*, i) said bryophyte cell further comprising any functional human beta-1,4-galactosyltransferase including variants, mutants and recombinants capable of producing any human glycosylation pattern (as in claims 40, 42, 83 and 84) and ii) any bryophyte plant or bryophyte tissue comprising said transformed *Physcomitrella patens* (as in claims 78 and 87; also see 112 second paragraph rejection for claim interpretation), is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir, 1988).

In support of their request that the prior rejection of claims 40, 42, 78 and 83-87, under 35 U.S.C. 112, first paragraph for enablement be withdrawn, applicants' have not provided any arguments with regard to claims 40, 42, 78, 83, 84 and 87.

Therefore, for the reasons of record and those set forth above, one cannot reasonably conclude that the full scope of the claimed invention is enabled by the teachings of the specification and/or the prior art.

Written Description

Claims 40, 42, 78 and 83-87 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 40, 42, 78 and 83-87, as interpreted are directed to a transformed bryophyte from *Physcomitrella patens* comprising extremely large number polynucleotides and encoding polypeptides of undefined structure said polypeptides having a functional human beta-1,4-galactosyltransferase including variants, mutants and recombinants capable of producing any human glycosylation pattern and furthermore any bryophyte plant or bryophyte tissue comprising said transformed *Physcomitrella patens* (also see 112, second paragraph for claim interpretation).

In *University of California v. Eli Lilly & Co.*, 43 USPQ2d 1938, the Court of Appeals for the Federal Circuit has held that "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials". As indicated in MPEP § 2163, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that Applicant was in possession of the claimed genus. In addition, MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

In the instant case, there are no structural limitations or structure-function correlation recited in claims with regard to: a transformed bryophyte from *Physcomitrella patens*, i) said bryophyte cell further comprising any functional human beta-1,4-galactosyltransferase including variants, mutants and recombinants capable of producing any human glycosylation pattern (as in claims 40, 42, 83 and 84) and ii) any bryophyte plant or bryophyte tissue comprising said transformed *Physcomitrella patens* (as in claims 78 and 87; also see 112 second paragraph rejection for claim interpretation). While the specification in the instant application discloses a specific bryophyte *Physcomitrella patens* wherein in said *Physcomitrella patens* the endogenous gene encoding for alpha 1, 3-fucosyltransferase (FucT, 1711 bp, GenBank: partial cDNA: AJ429145, page 32 of specification) disrupted through targeted insertion by primer sequences SEQ ID NO: 48, 49, 50 and 51 or an endogenous gene encoding for beta 1,2 xylosyltransferase (XylT, 1788 bp, GenBank: corresponding to the coding region: AJ429144, page 38 of specification) disrupted through targeted insertion by primer sequences SEQ ID NO: 67, 68, 69 and 70 (page 39 of specification) or a double knockout comprising said FucT and XylT disrupted through targeted insertion (double knockout, disrupting the coding regions of said genes, pages 44-45 of specification), further in said single knockout or double knockout *Physcomitrella patens* the gene encoding the human beta-1,4-galactosyltransferase catalyzing the following glycosylation pattern; UDP-galactose + N-acetyl-D-glucosaminylglycopeptide \rightleftharpoons UDP + beta-D-galactosyl 1, 4,-N-acetyl-beta-D-glucosaminylglycopeptide (GalT, GenBank X55415; page 41 of specification) has been integrated by homologous recombination

and said *Physcomitrella patens* comprising said gene knockout (FucT and XylT or double knockout) expressing the human GalT is transformed with an expression construct encoding the secretable/soluble form of human vascular endothelial growth factor (VEGF) and said VEGF comprising the specific human N-glycan glycosylation pattern as catalyzed by said GalT enzyme, it fails to provide any information as to a transformed bryophyte from *Physcomitrella patens*, i) said bryophyte cell further comprising any functional human beta-1,4-galactosyltransferase including variants, mutants and recombinants capable of producing any human glycosylation pattern (as in claims 40, 42, 83 and 84) and ii) any bryophyte plant or bryophyte tissue comprising said transformed *Physcomitrella patens* (as in claims 78 and 87; also see 112 second paragraph rejection for claim interpretation). Due to the lack of description of any additional species/variants/mutants/recombinants of any functional human beta-1,4-galactosyltransferase including variants, mutants and recombinants capable of producing any human glycosylation pattern i.e., structure-function correlation of polynucleotides and encoding polypeptides by any identifying characteristics, one of skill in the art would not recognize from the disclosure that Applicant was in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

In support of their request that the prior rejection of claims 40, 42, 78 and 83-87 under 35 U.S.C. 112, first paragraph, for insufficient written description be withdrawn

applicants' have not provided any arguments with regard to claims 40, 42, 78 and 83-87.

Therefore, for the reasons of record and those set forth above, one cannot reasonably conclude, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Summary of Pending Issues

The following is a summary of issues pending in the instant application.

- 1) Claims 40, 42, 78, 83, 84 and 87 depending therefrom are objected to because of informality.
- 2) Claims 48 and 50 are objected to as they depend from rejected base claims.
- 2) Claims 38-40, 42, 78, 81, 83, 84 and 89 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7, 16, 23, 24, 28 and 29 over co-pending US application 11/995,191.
- 3) Claims 40, 78, 84-87 and 96 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
- 2) Claims 40, 42, 78 and 83-87 under 35 U.S.C. 112, first paragraph, for enablement and insufficient written description.

Conclusion

Claims 38-40, 42, 48, 50, 78, 81-87 and 96 are objected/rejected for the reasons identified in the Rejections and Summary sections of this Office Action. Applicants must

respond to the rejections in each of the sections in this Office Action to be fully responsive for prosecution.

Final Comments

To insure that each document is properly filed in the electronic file wrapper, it is requested that each of amendments to the specification, amendments to the claims, Applicants' remarks, requests for extension of time, and any other distinct papers be submitted on separate pages.

It is also requested that Applicants identify support, within the original application, for any amendments to the claims and specification.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathirama Raghu whose telephone number is 571-272-4533. The examiner can normally be reached between 8 am-4: 30 pm EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300 for regular communications and for After Final communications. Any inquiry of a general nature or relating to the status of the application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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